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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,610	02/03/2006	Jiri Jan Krepinsky	14096.55USWO	7658

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EXAMINER

MARTIN, PAUL C

ART UNIT	PAPER NUMBER
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1657

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/18/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,610	KREPINSKY ET AL.	
	Examiner	Art Unit	
	Paul C. Martin	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 5-9, 12-14, 17-19 and 23-28 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-9, 12-14, 17-19 and 23-28 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/13/05, 4/7/05</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims 1-3, 5-9, 12-14, 17-19 and 23-28 are pending in this application and were examined on their merits.

Claim Objections

Claim 7 is objected to because of the following informalities: The word "containing" in line 3 of the claim should have been struck through to indicate deletion. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is drawn to the detection of a change produced by an aldehyde-detecting reagent as compared to a control, however it is unclear what form or manner the change encompasses. Claim 25 is rejected as being dependent upon rejected Claim 1.

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Claims 25 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 25 contains the negative limitation of performing a step in the method of Claim 1 without adding an enzyme, however Claim 26 specifies two particular enzymes. It is unclear whether Applicant's means to include an enzyme in the method of Claim 25 or not. The Examiner has interpreted the claims to indicate that an enzyme is added in step 25.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Shamsuddin (US 5,348,860).

Shamsuddin teaches a method of screening for a cancerous or precancerous condition in an organ other than the large intestine of a human being, comprising adsorbing a sample of proteinaceous secretion associated with that organ (discharge from the breast of a human female) onto a protein capturing water insoluble substrate, and treating the a sample with an aldehyde detecting reagent (basic fuchsin) to visually detect marker carbohydrates and wherein a portion of a sample which test negative in a first treatment is further assayed as a self-referencing control against false negatives (Column 14, Claim 19, Column 15, Claim 20 and Column 16, Claim 23).

Shamsuddin teaches the use of Schiff's reagent (basic fuchsin) and wherein detecting a magenta coloration is indicative of a cancerous or precancerous condition of a rectal mucus sample, the retesting of negative samples wherein after reaction with periodic acid and reacted with basic fuchsin a positive colorization from purple to magenta indicates that glycoprotein was obtained but is negative with respect to the presence of a marker carbohydrate and wherein the absence of magenta color means sampling error (Column 9, Lines 25-35 and Column 10, Lines 50-68).

It is inherent in the method of Shamsuddin that the visual detection of maker carbohydrates is accomplished by the visual detection of a colorimetric change wherein the colorimetric change is indicative of cancer or precancerous condition.

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Shamsuddin teaches wherein the water-insoluble support can be a membrane filter or solid beads of latex, glass or plastic (Column 7, Lines 2-6) and the use of the oxidative enzyme galactose oxidase (Column 16, Claim 21).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 5-8, 12, 14, 17, 23, 24 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shamsuddin (US 5,348,860).

The teachings of Shamsuddin were discussed above.

Shamsuddin does not teach a method wherein the sample is treated with Schiff's reagent without any pre-washing or wherein the sample of breast fluid is obtained from the nipple of one or both non-lactating breasts of the subject, or a kit for performing the assay.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of screening for a cancerous or precancerous condition in the discharge from the breast of a human female as taught by Shamsuddin above by obtaining the breast fluid from the nipple of one or both non-lactating breasts of the subject and directly treating the proteinaceous sample of breast fluid with Schiff's reagent without a pre-washing step because one of skill in the art would have recognized that a sample from a lactating individual would contain larger amounts of diluting and/or potentially interfering components in the form of fats, hormones, minerals. One of ordinary skill in the art would have recognized that directly obtaining the sample of breast fluid from the nipple would have been an easy and less invasive means of obtaining a sample, than say, a needle biopsy. One of ordinary skill in the art would have recognized that the direct treatment of the sample without a prior washing step, a result-effective adjustment of conventional working parameters (e.g., determining the optimal experimental conditions) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan. One of ordinary skill in the art would have recognized that although Shamsuddin does not teach a kit for performing the screening method, that the compilation of the necessary experimental or clinical components for performing the assay into a centralized location, or kit, giving the term its broadest, reasonable interpretation for purposes of convenience and efficiency would have been well within the purview of one of ordinary skill at the time of the instant invention.

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One of ordinary skill in the art would have been motivated to make these modifications in order to benefit from a less invasive means of obtaining a sample which is less likely to contain interfering or diluting components and a procedure which has been optimized for the best possible results. There would have been a reasonable expectation of success in making these modifications because the method of Shamsuddin teaches the obtaining of a breast fluid sample and a cancer or pre-cancerous detection method wherein the sample is washed prior to treatment with an aldehyde detection reagent.

Claims 1-3, 5-8, 12, 14, 17, 19, 24 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shamsuddin (US 5,348,860) in view of Sauter *et al.* (1999).

The teachings of Shamsuddin were discussed above.

Shamsuddin does not teach wherein the sample is additionally screened for the presence of other markers that are indicators of breast cancer.

Sauter *et al.* teaches the screening of nipple aspirate fluid for candidate biomarkers associated with breast cancer risk (Pg. 1224, Column 1, Lines 31-44 and Column 2, Lines 1-12).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the method of screening for a cancerous or precancerous condition in the discharge from the breast of a human female as taught by Shamsuddin above with the method of screening nipple aspirate fluid for candidate biomarkers associated with breast cancer risk as taught by Sauter *et al.* because both methods are directed toward the screening of breast fluid for biomarkers associated with cancerous or pre-cancerous conditions. One of ordinary skill in the art would have been motivated to combine these two methods because of the advantage of confirming a positive diagnosis based upon one assay with a confirmation diagnosis using a separate assay. There would have been a reasonable expectation of success in making this combination because both assays are directed to the screening of breast fluid for biomarkers associated with cancerous or pre-cancerous conditions.

Claims 1-3, 5-9, 12-14, 17, 18 and 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shamsuddin (US 5,348,860) in view of Krepinsky *et al.* (US 6,187,591 B1).

The teachings of Shamsuddin were discussed above.

Shamsuddin did not teach a method wherein the aldehyde marker comprises low molecular weight aldehydes that are soluble in water and are capable of reacting with Schiff's reagent to produce a colorimetric change, wherein the colorization is distinguished from other colorations, wherein the water insoluble substrate is made from polyester fiber or glass fiber fabrics, the treatment of the sample without a step of adding an enzyme (galactose oxidase or catalase) or wherein the aldehyde marker comprises aldehydes derived from plasmalogens.

Krepinsky *et al.* teaches the detection of aldehydes derived from plasmalogens in colorectal mucus by reaction of the aldehydes with Schiff's reagent to produce a colorimetric change (Column 6, Lines 38-52) and wherein the colorization is distinguished from other colorations (Column 6, Lines 50-63).

Krepinsky *et al.* teaches that low molecular weight, aliphatic aldehydes can be removed by aqueous washing (Column 6, Lines 64-67 and Column 7, Lines 1-3) the use of a water insoluble substrate made from polyester fiber or glass fiber fabrics (Column 7, Lines 64-67 and Column 8, Line 1) and the treatment of the sample without a step of adding an enzyme (Column 8, Lines 6-16).

Krepinsky *et al.* teaches the method of detection offers improved specificity reduction in false positives and negative diagnosis (Column 6, Lines 38-63).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the method of screening for a cancerous or precancerous condition in the discharge from the breast of a human female as taught by Shamsuddin above with the method of Krepinsky *et al.* for the detection of aldehydes derived from plasmalogens because both methods are directed to similar means of detecting cancerous and pre-cancerous conditions by the reaction of aldehyde markers in a proteinaceous sample with Schiff's reagent. One of ordinary skill in the art would have recognized that as it was known in the art that water soluble, low molecular weight aldehydes derived from plasmalogens were known to be removed by water washing that these aldehydes can be detected via reaction with Schiff's reagent if no washing step were performed. One of skill in the art would have recognized that the colorimetric change would have to be distinguished from other colorations as described by Krepinsky *et al.* in order to ascertain a successful positive, negative or false-negative colorization. One of ordinary skill in the art would have been motivated to combine these two methods because of the advantages described by Krepinsky *et al.* of improved specificity in diagnosis of a cancerous or pre-cancerous condition. There would have been a reasonable expectation of success in making this combination because both methods are directed to the detection of a cancerous or pre-cancerous condition by the detection of a colorimetric reaction of aldehydes in proteinaceous samples with Schiff's reagent.

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From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

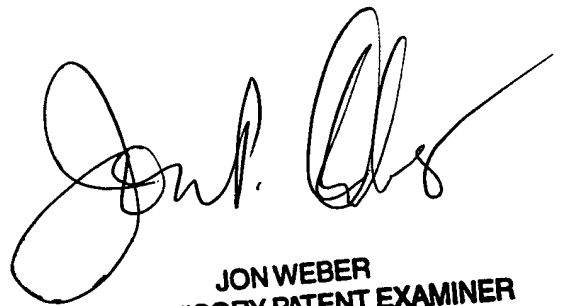
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

12/08/06



JON WEBER
SUPERVISORY PATENT EXAMINER